

## A case of metastatic pancreatic tumor prepared for surgery by applying therapeutic plasmapheresis due to hyperthyroidism

Hyperthyroidism controlled with plasmapheresis in pancreatic cancer

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### Abstract

A 64-year-old male patient admitted with complaints of nausea, vomiting, fever, and itching. After evaluation with laboratory tests and magnetic resonance cholangiopancreatography, a stent was placed in the common bile duct with Endoscopic retrograde cholangiopancreatography due to common bile duct constriction without tumoral pathology. After 7 days of follow-up, the patient was discharged. Five months later, the patient admitted with similar symptoms. In imaging tools, a mass located in ampullary area without metastasis was found. Surgery was planned for the patient. Unresectable pancreatic head tumor and millimetric liver metastasis were detected during surgery. A biopsy was taken from both the liver and the pancreatic mass, and the operation was terminated. Two months after surgery, the patient was admitted again with obstructive symptoms. The patient had hyperthyroidism on laboratory evaluation. Antithyroid drugs were started, but they were not effective. Therefore, 3 sessions of plasmapheresis were performed to provide euthyroidism to the patient. The patient, who underwent non-resective surgery, was discharged on the 22nd postoperative day.

### Keywords

Hyperthyroidism, Plasmapheresis, Intestinal Obstruction, Operation

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## Introduction

Three treatment options are conventionally used in the treatment of hyperthyroidism: Anti-thyroid drugs, radioactive iodine therapy, and surgery. Anti-thyroid drugs are a safe first-line treatment for most patients. With anti-thyroid drugs, it is aimed to reduce blood thyroid hormone levels and the effects of these hormones. It is also aimed to release thyroid hormones into the blood circulation and prevent their peripheral effects. However, serious side effects such as hepatotoxicity and agranulocytosis can develop due to anti-thyroid drugs [1].

Drugs cannot be used effectively in intestinal obstruction cases. It has been reported that therapeutic plasmapheresis is an effective treatment option in cases where traditional treatment methods are ineffective or cannot be used in the short term for the patient to create euthyroidism before the surgery [2].

In this case report, we aimed to present a hyperthyroid patient with duodenal obstruction due to a periampullary tumor. Since hyperthyroidism cannot be controlled with anti-thyroid drugs and emergency surgery is required for the patient, therapeutic plasmapheresis was used to provide euthyroid state.

## Case Report

A 64-year-old male patient was admitted to the Department of Gastroenterology, Erzurum Regional Education and Research Hospital, Erzurum, Turkey with complaints of nausea, vomiting, fever, oral intake disorder and itching in January 2020. In his medical history, the patient had hypertension, diabetes mellitus and goitre. He was taking propylthiouracil (50-milligrams tablets every 8 hours) in addition to anti-hypertensive drugs and antidiabetic drugs. There was no history of surgery.

On evaluation, the vital findings of the patient were as follows: blood pressure: 114/62 mm Hg, pulse rate: 118 beats per minute, oxygen saturation on room air: 96%, and body temperature: 38.1° Celsius. The patient's sclera was icteric, his skin appeared yellowish. On abdominal physical examination, the patient had abdominal pain in deep palpation in the right upper quadrant. Digital rectal examination was also normal. Other system examinations were normal.

The patient's pathological laboratory parameters were as follow: white blood cell count:  $11.8 \times 10^3/\text{mm}^3$ , alanine aminotransaminase (ALT): 217 U/L [0-55], aspartate aminotransaminase (AST): 65 U/L [5-34], alkaline phosphatase (ALP): 321 U/L [40-150], gamma glutamyl transferase (GGT): 621 U/L [12-64], total bilirubin (TB): 8.2 mg/dL [0.3-1.2], and direct bilirubin (DB): 5.2 mg/dL [0-0.5]. Other laboratory parameters were not remarkable, including tumor markers.

On magnetic resonance cholangiopancreatography (MRCP) scan, gallbladder was hydropic. Common bile duct diameter increased (up to 12 millimeters). Endoscopic retrograde cholangiopancreatography (ERCP) was applied to the patient. During ERCP, it was observed that the distal common bile ducts ended bluntly without tumoral pathology. A stent was placed in the common bile duct with ERCP. The patient was consulted to the general surgery clinic, and control was recommended 10 days later in order not to miss the possibility of any tumor and to renew the tests. After 7 days of follow-up, when the patient's bilirubin values decreased, the patient was discharged, and control was recommended. Since the beginning of the

COVID-19 pandemic, the patient has not been able to apply to the hospital for control. We determined that the patient did not come for control.

The patient admitted with similar symptoms in June 2020 at our clinic. On evaluation, the vital findings of the patient were as follows: blood pressure: 134/82 mm Hg, pulse rate: 98 beats per minute, oxygen saturation in room air: 95%, and body temperature: 37.2° Celsius. The patient's sclera was icteric. On abdominal physical examination, the patient had abdominal pain with deep palpation in the right upper quadrant. A digital rectal examination was also normal. Other system examinations were normal. In laboratory findings, patient's pathological laboratory parameters were as follow: ALT: 135 U/L [0-55], AST: 80 U/L [5-34], ALP: 221 U/L [40-150], GGT: 381 U/L [12-64], TB: 4.2 mg/dL [0.3-1.2], and DB: 2.2 mg/dL [0-0.5]. Other laboratory parameters were not remarkable, including tumor markers.

A lesion with a size of 15 millimeters was observed in the periampullary area in the distal part of the common bile duct, and MRCP was planned for the patient. On MRCP, gall bladder was hydropic. The common bile duct diameter was enlarged, and a stent was seen inside. There was a mass of approximately 22\*16 mm in size in the periampullary area. Positron emission tomography (PET) was planned for the patient. On PET scan, there was a mass of approximately 22\*18\*36 mm in size in the periampullary area (SUV-MAX: 6.59) with heterogeneous hypermetabolic lymph nodes in millimetric sizes (SUV-MAX: 5.36). No distance metastasis was seen on the PET scan. Therefore, surgery was planned for the patient with a diagnosis of periampullary tumor. The surgery was started with a midline upper umbilicus incision. Examination revealed multiple millimetric nodular liver lesions. The gallbladder was hydropic, and there was an immobile lesion at pancreaticoduodenal junction. The mass was considered to be unresectable, and the operation was terminated after cholecystectomy and wedge biopsy from both the liver and the mass. After 2 days of follow-up in the service, the patient was discharged. In pathological evaluation, liver biopsy was consistent with adenocarcinoma metastasis, while pancreatic biopsy was consistent with dysplasia. In addition, the gallbladder pathology was consistent with chronic cholecystitis. Therefore, the patient was referred to oncology for chemotherapy.

Two months after the operation, the patient applied to our clinic again with abdominal pain, fever, vomiting and nausea. When evaluated, the vital findings of the patient were as follows: blood pressure: 94/58 mm Hg, pulse rate: 114 beats per minute, oxygen saturation in the room air: 93%, and body temperature: 37.9° Celsius. On physical examination, the patient had severe cachexia with conjunctival icterus. The thyroid gland was palpable with pain. On physical examination of the abdomen, the patient had abdominal pain with deep palpation in the right upper quadrant.

In laboratory findings, the patient's pathological laboratory parameters were as follow: White blood cell count:  $13.4 \times 10^3/\text{mm}^3$ , hemoglobin level: 8.2 g/dL [14.1-17.8], ALT: 85 U/L [0-55], AST: 45 U/L [5-34], ALP: 254 U/L [40-150], GGT: 531 U/L [12-64], TB: 2.1 mg/dL [0.3-1.2], DB: 0.9 mg/dL [0-0.5], thyroid stimulating hormone (TSH): 0.01  $\mu\text{IU/mL}$  [0.55-4.78], freeT4: 2.23 ng/dL [0.70-1.48]. Other laboratory parameters

**Table 1.** Measurements after the 1<sup>st</sup> session

Explanations	Measured Value	Normal Range
TSH	(0.24) ul/ml	(0.55-4.78) ul/ml
FT3	(6.54) pg/ml	(2.3-4.2) pg/ml
FT4	(2.71) ng/dl	(0.89-1.76) ng/dl

**Table 2.** Results of the 2<sup>nd</sup> session after the application of plas-mapheresis, after 48 hours

Explanations	Measured Value	Normal Range
TSH	(0.39) ul/ml	(0.55-4.78) ul/ml
FT3	(6.39) pg/ml	(2.3-4.2) pg/ml
FT4	(1.77) ng/dl	(0.89-1.76) ng/dl

**Table 3.** Measurements after the last session (3<sup>rd</sup> session)

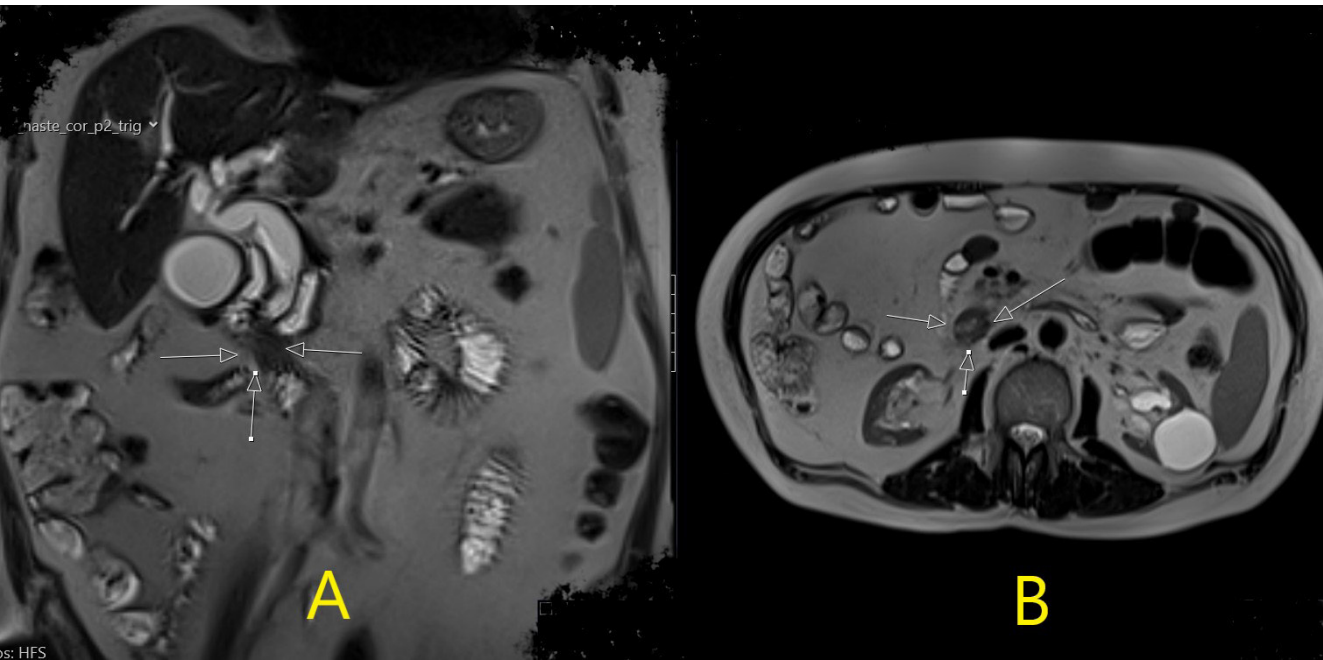
Explanations	Measured Value	Normal Range
TSH	(0.45) ul/ml	(0.55-4.78) ul/ml
FT3	(5.26) pg/ml	(2.3-4.2) pg/ml
FT4	(1.62) ng/dl	(0.89-1.76) ng/dl

were not remarkable. MRCP was taken to patient. On MRCP, the gallbladder was hydropic. The common bile duct diameter was enlarged, and a stent was seen inside. There was a mass of approximately 27\*22 mm in size in the periampullary area (Figure 1).

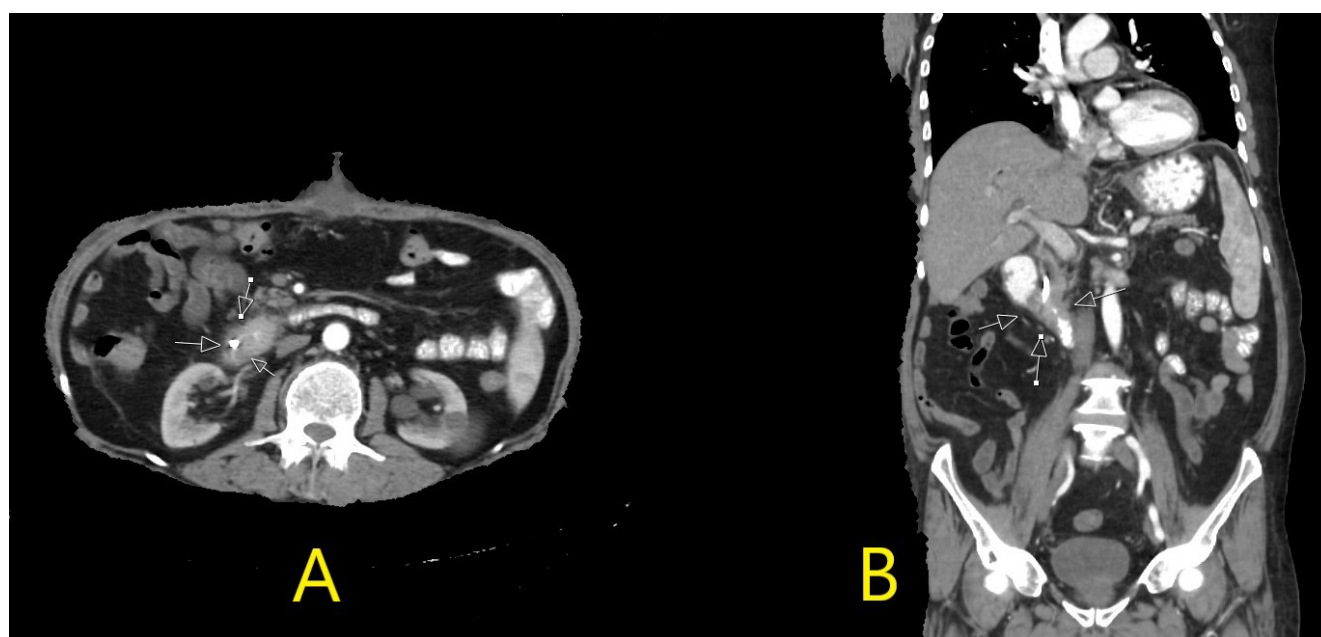
The patient was hospitalized with the diagnosis of cholangitis. Oral intake was stopped. Intravenous fluid replacement was started. The nasogastric catheter was inserted due to the severe vomiting of the patient. Intravenous piperacillin-tazobactam (4.5-gram vial every 8 hours) and intravenous metronidazole (500 mg/100 mL every 8 hours) were started. Due to the abnormal thyroid function tests, the patient’s anti-thyroid treatment was arranged. The propylthiouracil dose was

increased to 100 mg tablets every 8 hours, and propranolol (40 mg tablets every 12 hours from the nasogastric tube) was started. Supraventricular tachycardia (170-180 beats per minute) occurred on the third day of admission. There was no pathology in cardiac evaluation with echocardiography. The patient was transferred to the intensive care unit for follow-up. Heart rate was taken under control with diltiazem intravenous slow infusion. On the fifteenth day of admission, the thyroid function tests were as follows: TSH: 0.00  $\mu$ U/mL [0.55-4.78], freeT4: 2.38 ng/dL [0.70-1.48]. Contrast-enhanced abdominal CT was planned for the patient in order to evaluate the digestive system passage due to the prominence of thyrotoxicosis, despite anti-thyroid therapy on the 10th day of his admission. On CT scan, there was almost complete obstruction due to a tumor (Figure 2). A diversion surgery was planned for the continuity of the digestive system. Therapeutic plasmapheresis was started because hyperthyroidism poses a high risk for surgery. After 3 sessions of plasmapheresis with fresh frozen plasma, the patient’s thyroid function tests were as follows: TSH: 0.45  $\mu$ U/mL [0.55-4.78], freeT4: 1.62 ng/dL [0.70-1.48].

The patient was taken to emergency surgery. Examination revealed an immobile lesion surrounding the third part of the duodenum. Diversion surgery was planned. Gastrojejunostomy, choledocojejunostomy and jejunojejunostomy were performed. One of the drains was placed in the subhepatic area and the other in the pelvic cavity. The patient was followed up in the intensive care unit after surgery. Oral intake was started on the postoperative third day. Propylthiouracil treatment was continued with 100 milligrams tablets every 8 hours. Klebsiella pneumoniae grew in the culture examination of intraoperative choledochal bile sample, and amikacin intravenous vial (500 mg/2 mL started every 12 hours). As the patient had persistent fever, contrast-enhanced thorax and abdominal CT scan was performed on the postoperative fifth day. The patient had bilateral pleural effusion and atelectasis on CT scan without abdominal pathology. Escherichia coli grew in the blood culture on the postoperative eighth day, and meropenem 1 gram



**Figure 1.** On MRI scan before surgery, a mass was shown with arrows. (A: Coronal section, B: Axial section).



**Figure 2.** A 64-year-old male patient with metastatic peri-ampullary tumor was admitted. He also had goitre with hypothyroidism. On CT scan before surgery, a mass was shown with arrows. (A: Axial section, B: Coronal section).

vial every 8 hours was started. All drains were removed on the 10th postoperative day, and the patient was transferred to the service for follow-up. On the postoperative 12<sup>th</sup> day, a peri-umbilical abscess was seen, and this abscess was drained. Antibiotherapy was completed according to the culture results. The patient was discharged on the 22<sup>nd</sup> postoperative day with propylthiouracil (50 mg tablets every 8 hours). No complications were detected in the patient's follow-up 1 month after discharge. Chemotherapy treatment was started again.

### Discussion

Plasmapheresis is a treatment method based on taking whole blood out of the body and separating it into plasma and shaped elements with the help of a plasmapheresis device and re-circulating shaped elements with replacement fluid [3]. The purpose of this method is to quickly remove protein-derived hormones, harmful plasma components, immune complexes and toxins from the circulation. Since most thyroid hormones are bound to plasma proteins in blood circulation, plasmapheresis allows dilution of the concentration of free thyroid hormones. But the therapeutic effect of plasmapheresis is temporary.[4] Plasmapheresis was first shown in a case of thyrotoxicosis that the thyroid hormone level was decreased successfully after plasmapheresis in 1970 [5]. Subsequently, case reports have been published showing that thyroid hormone levels decrease rapidly with therapeutic plasmapheresis applications and a successful clinical response occurs [6]. In the last published American Apheresis Association guideline, it is recommended that the treatment decision should be personalized because the optimal role of therapeutic plasmapheresis in thyrotoxicosis is not fully determined. In the same guideline, clinical improvement can be seen before the decrease in hormone levels, therefore it is recommended to continue plasmapheresis every 2-3 days. Instead of replaced plasma, albumin, fresh frozen plasma, hydroxyethyl starch (HES) or their mixture is used as replacement fluid [4]. Fresh frozen plasma was used as

a replacement fluid in this patient.

Fever, urticaria, hypotension, paresthesia due to citrate, decrease in coagulation factors and immunoglobulins and infection transmission risk may be observed depending on the replacement fluid. Rarely, anaphylactoid reactions, resulting from the use of fresh frozen plasma, constitute the most serious complication of plasmapheresis. It is the leading cause of death due to plasmapheresis [7]. In our patient, no complications related to the procedure were observed during three sessions of plasmapheresis.

An important advantage is that fresh frozen plasma is inexpensive and easy to obtain. A review of reported complications from over 15,000 plasma exchange treatments found that adverse reactions were substantially more common with fresh frozen plasma than with albumin replacement (20 versus 1.4 percent) [8].

In conclusion, in our case, effective results were obtained in laboratory and clinically with therapeutic plasmapheresis. It is not a frequently preferred method due to its expensive, invasive nature and technical limitations. Therapeutic plasmapheresis can be a method that can be used as an alternative or additional treatment to standard treatments in cases where primary treatment options are contraindicated or ineffective in the stage of preparing severe hyperthyroid patients for the operation.

### Scientific Responsibility Statement

*The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.*

### Animal and human rights statement

*All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

#### **Conflict of interest**

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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